Chapter 1

In diabetic condition or in autonomic neuropathy a hormonal imbalance exists with decreased insulin secretion and increased levels of CA, glucocorticoids and growth hormone. These in turn have effects on the general metabolism of the body and of specific tissues. The changes are reflected in the body weight and also in tissue size and weight and water content. Since kidney plays an important role in both excretion and metabolic homeostasis, various experimental groups were formed to find out changes in these parameters in the kidney. The present chapter deals with the results of these experiments. Body weight showed a non-significant change in the VGX rats, whereas it decreased in ADX and ADX + VGX rats. In the CSX, CSX + ADX and CSX + VGX rats, an increase was observed in the body weight over the tenure of the treatment, but this increase was not as significant as in the control rats. Renal weight increased in groups in which vagotomy was performed (VGX, VGX + ADX, CSX + VGX). Though there was an accelerated catabolic condition in the tissue, the weight increased, which led to the inference that this could be because of the probable beginning of renal hypertrophy, a common feature in diabetics with nephropathy. CSX rats showed an increase in the renal weight, which could be because of the reduced mobilization. But in ADX and CSX + ADX rats, there was a significant decrease in renal weight, despite the reduced mobilization. This could be because of decreased water content observed in the ADX, VGX + ADX and CSX + ADX rats. In CSX and CSX + VGX rats, the water content increased, whereas VGX animals showed no significant change.
Chapter 2

Metabolic homeostasis is regulated in the body by the autonomic nervous system. The parasympathetic system causes the uptake and utilization of the glucose, whereas the sympathoadrenal system influence is exerted by breaking down the stores of the body. This can be accomplished either by the direct innervation of tissues or through the hormones. Apart from its excretory function, kidney also plays an important part in glucose homeostasis. The present chapter incorporates the results of the experiments which were carried out to observe the effect of parasympathetic denervation and adrenal ablation, singly and in combination, on the metabolic profile of the kidney.

VGX rats manifested a hyperglycemia. Looking into the various parameters of glucose metabolism in the kidney, it was observed that glycogenesis decreased, whereas glycogenolysis increased, this could be inferred from the depleted glycogen deposits in the kidney and a concomitant decline in the activity of glycogen synthase. Glycogen phosphorylase showed a high activity in the kidney, a condition subsequently promoting hyperglycemia. This condition was also favored by a rise in the gluconeogenic rate, reflected in the intensified activity of G-6-Pase, and also LDH. Lipid content also decreased in this condition indicating decreased deposition and also increased lipolysis. Oxidative metabolism of the tissue increased as demonstrated by high SDH activity. AChE activity declined indicating the success of vagotomy. On the other hand, when adrenalectomy was performed in the rats, a hypoglycemia was attained. Glycogenesis was on a rise, with a lowered glycogenolysis. The gluconeogenic rate also declined considerably, with low G-6-Pase activity, but not that of LDH. Lipolysis did not occur, and SDH activity decreased, restricting the oxidative metabolism in the kidney. AChE activity increased in the kidney. In the VGX + ADX animals, a marginal hyperglycemia was observed. The glycogen content was reduced, and this was more because of an increased breakdown than a decreased deposition, because glycogen synthase did not decrease, whereas phosphorylase activity increased. Though the gluconeogenic rate remained higher than the control level, it was not as significantly high as in the VGX rats. Lipid content also did not decrease as significantly as it did in the VGX animals. SDH activity was also reduced, as did the activity of AChE.

The results thus lead to a conclusion that the metabolic disturbances leading to a hyperglycemic state after vagotomy, can be corrected to a certain extent by performing...
adrenalectomy in these rats, as it brings about a check in the breakdown of the storage products.

Chapter 3

The autonomic nervous system has been implicated in the regulation of gluconeogenesis via amino acid metabolism, as insulin, glucagon, catecholamines and glucocorticoids have important influences in the state of protein metabolism. The present investigation was conducted by carrying out vagotomy and adrenalectomy in rats. Activities of the enzymes involved in transamination as well as those concerning transport and uptake of glucose, and the total protein content of the renal tissue were measured to scrutinize changes if any after the neuroendocrine manipulation.

Vagotomized animals showed a decreased protein content in the kidney. Both aspartate and alanine transaminases showed increased activity. This indicated an increased protein breakdown and amino acid mobilization via the transamination pathway. In conjunction with this, the lysosomal enzyme acid phosphatase showed a rise in the activity, supporting proteolysis. Transport enzyme alkaline phosphatase exhibited a decrease, resulting in decreased uptake of glucose and amino acids. Na⁺-K⁺-ATPase, the membrane bound enzyme showed an increased activity which seems to contradict some findings showing an increase in the activity of this enzyme caused by insulin. This was despite the enhanced catabolic state if this condition. Therefore the reason for the increase in the high activity of this enzyme could be the beginning of renal hypertrophy, in which this enzyme is involved. ADX animals, manifested a different picture with increased protein content in the tissue and in turn decreased transamination, with reduced acid phosphatase activity. Alkaline phosphatase activity increased causing a rise in the uptake of glucose and amino acids. This is also reflected by hypoglycemic state. Na⁺-K⁺-ATPase activity showed a reduced activity indicating the absence of the positive influence of adrenal steroids and catecholamines on this enzyme. In the VGX + ADX animals again the protein content declined with, transamination from alanine being curtailed. Acid phosphatase also declined, as did the alkaline phosphatase activity, supporting the marginal hyperglycemia.

It can thus be concluded that the hyperglycemic state found in the VGX rats is also supported by protein breakdown and gluconeogenesis as well as decreased uptake of
metabolites. This can be improved upon by performing adrenalectomy in these rats, which curtails the protein breakdown, an important feature of the body wasting found often in the diabetic patients.

Chapter 4
The sympathoadrenal system mediates the counterregulation of hypoglycemia through the genesis of hyperglycemia by causing glucose mobilization from the carbohydrate and non-carbohydrate sources. This is done by sympathetic neurotransmitters through direct innervation to the kidney and the adrenal hormones. In this chapter, results of chemical sympathectomy by means of an antiadrenergic drug guanethidine, singly and in combination with adrenalectomy and vagotomy have been discussed.

The chemically sympathectomized animals manifested a lowered blood glucose level. This state of glycemia is a consequence of increased glycogenesis and reduced glycogenolysis. G-6-Pase, the gluconeogenic enzyme also decreased. LDH however showed no reduction in the activity. SDH activity was reduced, indicating a decrease in the oxidative metabolism of the renal cells, possibly caused due to lack of catecholamines after chemical sympathectomy. The lipid content of the tissue increased, indicating lipid deposition and not lipolysis. An enhanced parasympathetic tone is manifested by increased AChE. When vagotomy was performed in these animals, the glycemic state was slightly elevated, as a consequence of decreased deposition of and increased lysis of glycogen. G-6-Pase showed only a small increase, lipid content was also depleted slightly. Activities of both the dehydrogenases showed no departure from the control levels. AChE activity also decreased. Conversely, when adrenalectomy was performed in the CSX animals, the hypoglycemia was heightened, the glucose nadir that was attained was much more significant than in the animals with CSX alone. Glycogenesis increased, whereas glycogenolysis and gluconeogenesis declined markedly. Only the LDH activity showed an increase. SDH activity decreased, implying low oxidative metabolism in the kidney. Lipolysis was also checked. AChE activity noticeably increased after CSX + ADX.

To summarize, it has been found that blockade or ablation of either of the division of the sympathoadrenal system is not able to counterregulate the hyperglycemia produced by
vagotomy, to a very significant degree. However, when CSX and ADX were performed in combination, the hyperglycemic state was found to be reversed more significantly.

Chapter 5

The catecholamines are known to have an important influence in the protein metabolism directly and by causing an enhanced secretion of the pancreatic hormone glucagon. Increased concentration of glucagon, CA and glucocorticoids relative to insulin is believed to change metabolic processes away from anabolism towards catabolism. In the present chapter therefore, experiments were carried out by executing chemical sympathectomy alone and in combination with vagotomy and adrenalectomy to find out the counteracting influences that these systems have on the protein metabolism of the kidney, and if changes occur in the transport enzyme activities of the renal membranes.

Chemically sympathectomized animals showed an increase in the protein content with a reduced transamination and hence amino acid mobilization. Concomitantly acid phosphatase activity decreased in the kidney. Glucose and amino acid uptake increased, as can be observed by the high activity of alkaline phosphatase. Na⁺ K⁺ ATPase activity showed a decrease, probably due to the decreased glucose delivery of glucose to the renal tubules. When VGX was performed in the CSX animals, there was an increase in the protein content of the kidney, which was not as significant as in the kidney of the CSX rats. Here transamination from both alanine and aspartate was reduced, the reduction in AST being more pronounced. Acid phosphatase simultaneously declined. Both the transport enzymes showed a reduced activity. When adrenalectomy was performed in the CSX rats, the protein content was elevated very prominently, with a reduction in the activities of both the transaminases, thus indicating low protein mobilization. Acid phosphatase activity also was lowered, as was the Na⁺-K⁺-ATPase. Alkaline phosphatase activity increased showing an increased uptake of metabolites.

The results from the present chapter suggest that the reduction in protein degradation after CSX and CSX + ADX would be in large measure due to the influence of insulin on these pathways, uncountered by either catecholamines, glucagon or glucocorticoids.
Chapter 6
In conjunction with the autonomic nervous system, the endocrine glands of the body play an important role in the regulation of glucose homeostasis. Both these systems have an intricate relationship, regulating the functioning of each other. A delicate balance is maintained between the two. This chapter has an account of the effect of autonomic nervous system manipulation on the functioning of the pituitary-adrenocortical axis, a very important component of the endocrine system. Corticosterone and ACTH were measured in serum of the rats after various treatments.

VGX rats showed an increase in the corticosterone level whereas the ACTH concentration in the serum decreased. In the ADX rats, loss of the adrenal gland was manifested by a steep decline in corticosterone concentration in serum, ACTH level increased. In the VGX + ADX rats also a similar trend was observed. CSX rats also showed a reduced corticosterone concentration but this was not as significant as in ADX. ACTH level increased significantly. CSX + VGX rats manifested an increase in both corticosterone and ACTH concentrations. CSX + ADX rats showed a similar trend with corticosterone being decreased more significantly than in CSX alone.

To sum up, rats in which vagotomy was performed singly and in combination with CSX, glucocorticoid secretion increased, representing the insulinopenic condition comparable with diabetes. In those groups where adrenal was removed, alone or in combination, a marked decrease was attained in the glucocorticoid secretion, the decrease being equally significant in ADX alone and in combination with VGX and CSX, and also more pronounced than in CSX alone. It can thus be inferred that modulating the function of the adrenal could be competent enough to check the hypercortisolemia often found in diabetics.

Chapter 7
Growth hormone as secretory product of the anterior pituitary has important biological activities. In addition to its growth promoting function, it has influences on the glucose metabolism. It has anti insulin activities, causing glucose release by mobilizing the carbohydrate and noncarbohydrate sources in the body. Its effect on protein metabolism is anabolic. In the present chapter, GH profiles in various conditions of neuroendocrine
maneuvers have been investigated by eliminating the different components of the autonomic nervous system, alone and in different combinations.

VGX rats manifested an increased GH level, as also did the animals with CSX + VGX and VGX + ADX. The latter two conditions did not show a very significant increase. CSX rats manifested a decrease in the level of GH in the serum. Rats with ADX and CSX + ADX showed a very pronounced decrease.

The increases in GH levels in groups where vagotomy was performed (VGX, VGX + ADX, CSX + VGX) indicates that vagal denervation seems to have a major effect on the status of this hormone. The decrease observed in CSX, ADX and CSX + ADX conditions could be because of the removal of catecholamines and glucocorticoids which have a stimulatory effect on the secretion of this hormone. It can be therefore concluded that rats with CSX + ADX combination are able to restrain the rise in GH level more efficiently than either CSX and ADX alone.